

What is claimed is:

1. A method of performing RNA interference, said method comprising exposing a double stranded polynucleotide to a target nucleic acid, wherein said double stranded
5 polynucleotide is comprised of a sense strand and an antisense strand, and wherein said sense strand is substantially nonfunctional.
2. The method according to claim 1, wherein said sense strand comprises at least one 2'-O-alkyl modification.
- 10 3. The method according to claim 2, wherein said sense strand comprises at least one cytosine- or uracil-containing nucleotide base, and said at least one cytosine- or uracil-containing nucleotide base has a 2'-O-methyl modification.
- 15 4. The method according to claim 2, wherein said 2'-O-alkyl modification is a 2'-O-methyl modification.
5. The method according to claim 4, wherein said at least one 2'-O-methyl modification is on the first, second, eighteenth and/or nineteenth nucleotide base.
- 20 7. The method according to claim 1, wherein the sense strand further comprises a 5' conjugate.
8. The method according to claim 7, wherein the conjugate is cholesterol.
- 25 9. The method according to claim 1, wherein the sense strand comprises a cap on its 3' end.
10. The method according to claim 9, wherein the cap is an inverted deoxythymidine or
30 two consecutive 2'-O-methyl modified.

11. The method according to claim 1, wherein said antisense strand comprises at least one modified nucleotide.
12. The method according to claim 11, wherein the at least one modified nucleotide is a
5 2'-halogen-modified nucleotide.
13. The method according to claim 12, wherein the 2'-halogen modified nucleotide is a 2'-fluorine-modified nucleotide.
- 10 14. The method according to claim 1, wherein the sense strand comprises one or more cytosine- and/or uracil-containing nucleotide bases, and each of said one or more cytosine- and/or uracil-containing nucleotide bases is 2'-fluorine modified.
- 15 15. A method of performing RNA interference, said method comprising exposing a double stranded polynucleotide to a target nucleic acid, wherein said double stranded polynucleotide comprises
- (a) a conjugate;
 - (b) a sense strand comprising at least one 2'-O-alkyl modification, wherein said sense strand is substantially nonfunctional; and,
 - 20 (c) an antisense strand comprising at least one 2'-fluorine modification, wherein said sense and antisense strands form a duplex of 18-30 base pairs.
16. The method according to claim 15, wherein said at least one 2'-O-alkyl modification is on the first, second, eighteenth and/or nineteenth nucleotide base.
- 25 17. The method according to claim 15, wherein the conjugate is a 5' conjugate.
18. The method according to claim 15, wherein the conjugate is cholesterol.
- 30 19. The method according to claim 1, wherein the sense strand further comprises a cap on its 3' end.

20. The method according to claim 19, wherein the cap is an inverted deoxythymidine or two consecutive 2'O-methyl modified.